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COMPUTER-AIDED SEARCH OF RIBOSE 5-PHOSPHATE AND ATP CONFORMATION IN THE ACTIVE SITE OF THE PHOSPHORYBOSYLPYROPHOSPHATE SYNTHETASE FROM THERMOPHILIC THERMUS THERMOPHILUS

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Phosphorybosylpyrophosphate synthetase (**PRPPS**) catalyze thesynthesis of 5-phosphoribosyl pyrophosphate (5-PRPP) by transferring the β,γ-diphosphoryl group of adenosine triphosphate (ATP) to the C1-hydroxyl group of ribose 5-phosphate(**R5P**) [1]. R5P is involved in different vital synthesis of purine and pyrimidine nucleotides, pyrimidine-containingenzyme cofactors, and the amino acids histidine andtryptophan processes [2]. Due to an important role in nucleotide synthesis PRPPS is a promissing target for biotechnology. PRPPS can be used in one stage of the nucleotide analogs synthesis, that can act as antiviral and antitumoral drugs [3]. This work is focused on the searching of the ligands (ATP and RP5) position in the active site of PRPPS from *Thermophilic Thermus Thermophilus* (PRPPS-TT) by using molecular dynamics methods for identifying amino acid residues, responsible for binding specificity of the ribose ring of RP5.

The first part of this work was molecular dynamic simulations of PRPPS from *E. Coli* (PDB ID: 4SU2) with substrates (ATP and RP5). Afterthe simulation process the resulting structure was aligned to PRPPS-TT (PDB ID: 5T3O). Thus the PRPPS-TT complex with substrates in the active site was created. The structure of the protein and ligands was parameterizated in charmm36 forcefield. TIP3P water model was chosen as a solvent. Energy minimization, equilibration andmolecular dynamics was carried out using GROMACS software. The length of the simulation was chosen to stabilize the RMSD of the protein and the RMSD of ligands.

Resultingatom trajectories were analyzed andamino acid residues in the active site of the protein, responsible for binding specificity of the ribose ring of RP5 and ATP were found.Thisdataincomplexwith protein specificity (by different sugars) analysis can help discover mutations of PRPPS-TT, useful for cascade strategy for the biosynthesis of biologically important nucleotides and potential drugs.

This work was carried out using high-performance computing resources of federal center for collective usage at NRC “Kurchatov Institute” [4].

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